

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY  
DEPARTMENT OF PESTICIDE REGULATION  
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA  
DISODIUM CYANODITHIOIMIDOCARBONATE

Chemical Code # 000967, Tolerance #50394  
SB 950 #658

Original: April 17, 2003

I. DATA GAP STATUS

Chronic toxicity, rat: Subchronic Dermal, rat	Data gap, no study submitted. No adverse systemic effects indicated in an upgradeable study
Chronic toxicity, dog:	Data gap, no study submitted
Oncogenicity, rat:	Data gap, no study submitted
Oncogenicity, mouse:	Data gap, no study submitted
Reproduction, rat:	Data gap, no study submitted.
Teratology, rat:	No data gap, no adverse effect
Teratology, rabbit:	No data gap, possible adverse effect
Gene mutation:	No data gap, no adverse effects
Chromosome effects:	No data gap, possible adverse effect
DNA damage:	Data gap, inadequate study
Neurotoxicity:	Not required at this time

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Toxicology one-liners are attached.  
All record numbers through 114094 were examined.  
\*\* indicates an acceptable study.

**Bold face** indicates a possible adverse effect.

File name: T030417

Original: J. Kishiyama and Gee, April 17, 2003

US Environmental Protection Agency issued a "Reregistration Eligibility Decision" in September of 1994. DCDIC is an antimicrobial pesticide with aquatic, non-food industrial uses.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

## CHRONIC TOXICITY, RAT

No study submitted.

Subchronic, dermal

020 130934 Siglin, J. C. "91-Day Dermal Toxicity Study in Rats with DCDIC." (Springborn Life Sciences Inc., SLS Study No. 3138.21, September 27, 1988.) DCDIC (lot # 220C. 32% by weight) was administered dermally for 6 hours/day, 5 days/week for 13 consecutive weeks to 10 Sprague-Dawley rats/sex/group. Doses were 0 (water), 25, 125, or 250 mg/kg. Test article was applied as a 10% solution (w/v) at volumes of 0.25, 1.25 and 2.50 ml/kg with control receiving 2.5 ml/kg of water. The report did not state whether the doses were corrected for purity of DCDIC. Doses were applied to approximately 10% of the body surface and was stated as held in skin contact with gauze but details were not included as to how the material was spread onto the skin. Also, it was not clear if the treatment area was occluded. Following each exposure, the test area was wiped with gauze soaked with water. Body weight, bodyweight gain and food consumption were slightly reduced for mid- and high-dose female groups. Females (5/10) exhibited a weakened/absent limb grasping response at 250 mg/kg/day. There were no effects in males. Skin irritation was transient and mild for mid and high-dose groups of both sexes and for low dose females. Dermal NOEL < 25 mg/kg/day (erythema). Slightly reduced total bilirubin, creatinine, and potassium values at the high dose were reported but probably not biologically meaningful. Systemic NOEL = 25 mg/kg/day for females and 250 mg/kg/day for males. UNACCEPTABLE. Possibly upgradeable with clarification of the preparation of the dosing material and the method by which it was applied. No adverse systemic effects. Mild dermal irritation at all doses in females. (Kishiyama and Gee, 4/16/03).

EPA: dermal NOEL < 25 mg/kg/day based on erythema and a systemic NOEL of 25 mg/kg/day based on lower body weight and food consumption.

## CHRONIC TOXICITY, DOG

No study submitted.

## ONCOGENICITY, RAT

No study submitted

## ONCOGENICITY, MOUSE

No study submitted

## REPRODUCTION, RAT

No study submitted.

#### TERATOLOGY, RAT

**\*\* 50394 - 016 114094** Rodwell, D. E. "Teratology Study in Rats with DCDIC." (Springborn Life Sciences Inc., SLS Study No. 3138.23, September 20, 1988.) DCDIC (lot # 220C, 32% by weight) was administered as a single daily dose by gavage on days 6 through 15 of gestation at doses of 0, 0, 2, 6, or 18 mg/kg/day to 28 mated female Sprague-Dawley rats/group. Doses were not corrected for chemical purity. Mean pre- and post-implantation loss were comparable across all groups, including 18 mg/kg/day. Maternal NOEL = 6 mg/kg/day (reduced bodyweight, bodyweight gain, food consumption, decreased activity and partial loss of hind limb mobility, hunched posture and unthrifty appearance). Developmental NOEL = 6 mg/kg/day (non-statistically significant increased incidence of litters with bent ribs and unossified hyoid (reported as due to severe maternal toxicity), slightly reduced fetal body weight (6%) as a possible treatment related effect). No adverse developmental effects. ACCEPTABLE. (Kishiyama and Gee, 4/15/03)

EPA: NOEL = 6 mg/kg/day.

50119 - 009 074327 Duplicate of the above study on DCDIC indexed as Busan 85 (2-hydroxypropyl methanethiosulfonate).

50119 - 009 074571 Rodwell, D. E. "Pilot teratology study in rats with DCDIC." (Springborn Life Sciences, Inc., SLS 3138.22, May 31, 1988) Test article was DCDIC, lot 220C. Groups of 8 presumptive pregnant Sprague-Dawley COBS®CD® rats were given doses of 0 (water), 100, 200, 400, 600 and 800 mg/kg/day in 10 ml/kg by oral gavage. Doses were not adjusted for chemical purity (32% by weight). Due to toxicity, this portion of the study was terminated before day 20. Six additional groups were given 0, 2, 5, 10, 15 and 20 mg/kg/day for 10 days, gestation days 6 through 15. C-sections were performed on day 20 and maternal and external fetal exams performed. Body weights were recorded during the study on days 0, 6, 9, 12, 16 and 20. Survival was 100%. Clinical signs of decreased activity (6/3, incidence/number of animals), partial loss of hind limb mobility (21/5), hunched posture (6/3) and rough coat (5/3) were noted at 20 mg/kg/day. Body weight gains were affected at 10 (days 6-9), 15 (6-9 and 12-16) and 20 (severe loss 6-9, 12-16 and 6-16) mg/kg/day. Corpora lutea count, implantation sites, viable fetuses, early and late resorptions and sex ratios were not affected by treatment at any dose, including 20 mg/kg/day. No dams had only resorptions. Fetal weights were slightly lower at 20 mg/kg/day (3.6 versus 3.8). Doses selected for the definitive study were 2, 6 and 18 mg/kg/day. No worksheet. (Gee, 4/17/03)

#### TERATOLOGY, RABBIT

**\*\* 50394 - 016 114091** Rodwell, D. E. "Teratology Study in Rabbits with DCDIC." (Springborn Life Sciences Inc., SLS Study No. 3138.25, December 8, 1988.) DCDIC (lot 220C, 32% by weight) was administered in a single daily gavage on days 6 through 18 of gestation at doses of 0, 0, 3, 10, or 30 mg/kg/day (not corrected for chemical purity) to 20 artificially inseminated female New Zealand White rabbits/group. Effects observed included reddish colored fluid in some high-dose cages, reduced activity and hairloss for mid and high dose groups, reduced body weight gain for high dose group, and treatment- related death of

one mid and two high dose does. Pregnancy rate was 20% lower (70%) for the high dose group than controls (90%). In addition, 2/18 and 4/14 mid- and high- dose pregnant does had total litter resorption. MATERNAL NOEL = 3 mg/kg/day. Litter size was reduced and reflected the increased incidence of early resorptions, pre- and post- implantation loss and reduced implantation sites for mid- and high- dose does. DEVELOPMENTAL NOEL = 3 mg/kg/day. No evidence of teratogenicity per se. It was, however, not clear whether the fetotoxicity/embryo lethality and preimplantation loss were due to maternal toxicity or to specific toxicity to the fertilized ovum. ACCEPTABLE. (Kishiyama and Gee, 4/15/03)

EPA: Maternal and developmental NOEL = 3 mg/kg/day (reduced activity, mortality, increased resorptions and decreased litter size).

50119 074566 Duplicate of the above study on DCDIC indexed as Busan 85 (2-hydroxypropyl methanethiosulfonate).

**50119 - 010 074572** Rodwell, D. E. "Pilot teratology study in rabbits with DCDIC." (Springborn Life Sciences, SLS 3138.24, May 31, 1988) DCDIC (lot 220C, 32% by weight) was given by oral gavage to groups of 6 artificially inseminated New Zealand White rabbits at doses of 0 (water), 5, 10, 20, 50 or 80 mg/kg/day, gestation days 6 through 18. These doses were not corrected for chemical purity. There were 3/6 deaths at 50 mg/kg/day and 6/6 deaths at 80 mg/kg/day. Body weight and clinical signs were recorded. Fetal weight and external appearance were evaluated. Maternal clinical signs at 50 and, with increased incidence, at 80 mg/kg/day included decreased activity, partial loss of front limb mobility, prostration, soft/few/no feces, inhibited blinking response and ocular discharge. At termination, there were 4, 4, 3, 4, 1 and 0 litters with viable fetuses. The other does were not pregnant or had total litter resorptions (0, 1, 2, 0, 1, 0). One abortion occurred at 5 mg/kg/day but was not considered related to treatment as none occurred at higher doses. Body weight gains were lower at 50 and 80 mg/kg/day. The data for pre- and post-implantation loss at the lower doses (5, 10 and 20 mg/kg/day) without overt maternal toxicity suggested that there may be an embryotoxic effect with DCDIC, although the data were limited by the number of pregnant does. Apparent maternal NOEL = 20 mg/kg/day (mortality, clinical signs); developmental NOEL < 5 mg/kg/day (embryotoxicity). The study was considered supplemental to the full rabbit teratology study and was used for dose selection. (Gee, 4/17/03)

## GENE MUTATION

\*\* 013 062457 Jagannath, D. R. "Mutagenicity test on DCDIC in the Ames *Salmonella*/Microsome Mutation Assay." (Hazleton Laboratories America, Inc., HLA Study No.: 9971-0-401, October 12, 1987) Disodium Cyanodithioimidocarbonate (DCDIC) lot 220C, 32% active ingredient, was used at concentrations of 0, 0.1, 1.0, 2.5, 5, 10, 25, 50, and 100 : l/plate with and without S9 mix and evaluated for mutagenicity with *Salmonella typhimurium* strains TA 1535, TA1537, TA1538, TA98, and TA 100. There were triplicate plates per concentration with two independent trials. The number of revertants increased for TA 1535 in the repeat test, therefore, two additional trials were performed with DCDIC (with and without S9) with TA 1535. There were no increases in revertants in either additional trial. DCDIC was not mutagenic. ACCEPTABLE. (Kishiyama and Gee, 4/14/03)

## CHROMOSOME EFFECTS

**\*\* 013 062458** Murli, H. "Mutagenicity test on DCDIC in an *In Vitro* Cytogenetic Assay Measuring Sister Chromatid Exchange Frequencies in Chines Hamster Ovary (CHO) Cells." (Hazleton Laboratories America, Inc., HLA Study No.: 9971-0-438, August 25, 1987) DCDIC (lot 220C, 32% from record 062447, sp. gr. 1.28) was tested at concentrations of 0, 10, 33.3, 100, 333, or 1000 : l/ml without S9, at 33.3, 100, 333, or 1000 : l/ml with S9 and repeated at 198, 298, 397, 496, or 595 : l/ml without S9 Mix for evaluating the potential to induce sister chromatid exchanges (SCE) in Chinese hamster ovary (CHO) cells. **DCDIC in the absence of metabolic activation was reported as positive for inducing chromatid exchanges in Chinese Hamster ovary cells.** ACCEPTABLE. (Kishiyama and Gee, 4/14/03)

#### DNA DAMAGE

013 062447 Cifone, M. A. "Mutagenicity test on DCDIC in the Rat Hepatocyte Unscheduled DNA Synthesis Assay." (Hazleton Laboratories America, Inc., HLA Study No.: 9971-0-447, November 11, 1987) DCDIC (lot 220C, 32% by weight) was evaluated for effects on DNA at concentrations of 0 (medium), 504, 1010, 2020, 3020, 4030, and 5040 : g/ml by measuring UDS in primary rat hepatocytes by autoradiography. There were triplicate coverslips per concentration with 50 cells evaluated per coverslip for a total of 150 per concentration in a single trial. Viability was determined by Trypan blue dye exclusion. DCDIC at 4030 : g/ml increased the percentage of nuclei (12.7%) containing  $\geq 6$  grains. The increase was reported as spurious and DCDIC evaluated as negative for UDS, due to the lack of a dose related trend and no significant increase in net nuclear grains. UNACCEPTABLE (No individual data). Upgradeable with submission of data for each coverslip, including cytoplasmic and nuclear grain counts. (Kishiyama and Gee, 4/14/03)

#### NEUROTOXICITY

Not required at this time.